

REPORT OF A CASE OF ANTHRAX.¹

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ON February 12, 1892, a man, aged forty-four years, came to the Surgical Out-patient Department of the Boston City Hospital.

Dr. G. H. Monks made the diagnosis of charbon on the left side of the patient's neck. The patient gave the following history:

Three weeks before entrance, while working as a longshoreman, he had handled foreign hides, but does not remember having or receiving any scratches upon the hands or neck. Five days ago he noticed a "pimple" over the upper part of the left sterno-cleido-mastoid. This was itchy, and toward night became painful. It increased in area, at the end of the second day the neck was considerably swollen. On the third day the neck was swollen down to the clavicle. Since the beginning of the second day the patient has felt miserable. His head has ached; he has been feverish; has been nauseated; and has vomited once. When first seen he complained more of general pains throughout his body than of the local condition of his neck.

He was a man who had apparently been in perfect physical condition previous to this illness. His skin was slightly yellowish; the eyes looked "muddy;" the tongue had a light, white coat; and there was a large swelling which occupied the left side of the neck and extended from the median line in front to the outer edge of the left erector spinæ behind, and from the ear to the base of the neck. This mass consisted of glands; was movable, semi-elastic, and had a elly-like feeling. Planted in the skin covering this mass, one and one-half inches below the ear, was a raised surface the size of a silver dollar and of a purplish red color, the centre of which was black and a quarter of an inch in diameter. About this lay a ring of pustules

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half an inch wide. The dimensions of the pustule were two by one and a half inches. This raised pustulo-vesicular surface was connected with an underlying, movable, indurated mass the size of a small lemon.

After some thought it was decided to wait twenty-four hours to see if the patient was growing better or worse. The inflammation in the neck at this time had existed for five days; the diagnosis was not absolutely certain, and the amount of glandular infiltration was so great as to require a more extensive operation than one would undertake for a less serious disease, and if it were not anthrax it might be hoped that the inflammation had reached a limit and that the patient would be better on the next day.

Eighteen hours later he was seen, and it was found that he was worse. The pustular area had not materially increased, but the glandular swelling of his neck had increased and extended, and there was a large area of glandular swelling extending on to the sternum and the left side of the chest. The whole left side of the neck and area over the sternum was covered by an erythematous blush. He said that he had had intense pain in the head since last evening; temperature 101° F. It was decided to interfere immediately with the pustule.

The patient was etherized, and as rapidly as possible the whole lemon-sized, indurated, inflammatory mass was excised, care being taken that the pustule did not contaminate the freshly wounded area. This left a circular hole three and a quarter inches in diameter and an inch and a half in depth. The vessels were secured; it was irrigated out with corrosive sublimate, 1 : 1000, dusted with iodoform, and packed with iodoform gauze. The patient made a good recovery from the ether, but the shock of the operation was so great that active stimulation was necessary. On the next day the patient felt much better, and his headache was all gone; temperature was 101° F. The erythema had entirely disappeared, and the glands over the sternum and left side of the chest had subsided. Four days after operation the greater part of the glandular enlargement of the neck had disappeared. From the eighth to the sixteenth day of the disease the patient had diarrhoea, and it is questionable whether it was not colliquative. For five days after operation the patient had to be catheterized, and the amount of urine was less than one-half the normal quantity.

On the ninth day the temperature became normal, and from that



FIG. 1.—A case of Anthrax.

time on there was no material rise in temperature. From the time of the operation on the sixth day to the twentieth day stimulants and nourishment were pressed. The deep circular hole did well, gradually filling with granulations, and was completely closed in sixty days after the operation. There is now a line of cicatrix two inches in length and a quarter of an inch in width running parallel with the left sterno-cleido-mastoid. It is attached to the underlying structures, and there is no sensation in the skin over the angle of the inferior maxilla. On trying to lift with the left arm there is some pain in the neck, which runs down the course of the median nerve. This does not interfere with his occupation.

Just before the operation Mr. Greenleaf R. Tucker, the chemist of the Boston City Hospital, made cultures of the fresh blood flowing from the wound. His report is as follows:

Bacteriological Report.—The following is a brief account of the anthrax bacillus and of the identification of the organism in the case of F. H., admitted to the Boston City Hospital February 12, 1892, with the provisional diagnosis of malignant pustule:

The anthrax bacillus is a comparatively large organism, readily seen in blood or in tissues containing it, with an objective of moderate power. It multiplies rapidly upon nutrient media at the ordinary temperature of the laboratory; Upon nutrient agar agar it grows rapidly, spreading out from the inoculation line over the whole surface, furnishing by its growth a mucilaginous product, not, however, especially characteristic. But in nutrient gelatin, if it be not too concentrated, and if the proper conditions are maintained, there appear somewhere along the inoculation line minute hair-like filaments, gradually increasing in number until the entire line is complete with them. They make their way progressively through the gelatin in a lateral direction until they meet with opposition in the sides of the tube. On longer standing the gelatin completely liquefies, resulting in a clear yellowish-brown liquid, while the products of the decomposition of the gelatin by the organism settle out. When perfectly developed, and before liquefaction sets in, the culture presents a highly characteristic feather-like appearance. Finally, the organism produces death in animals susceptible to its influence in from twenty-four to forty-eight hours.

All the above conditions were obtained by an organism fur-

nished by the serous fluid obtained from vesicles located upon the neck of F. H.

The organism was the bacillus anthracis, the cause of the disease known as malignant pustule. The various steps leading to the identification of the organism, and other incidental facts, are as follows:

The neck of the patient was carefully washed with a solution of corrosive sublimate 1 : 1000, followed by alcohol, after which several vesicles were punctured with a sterilized platinum wire, and the serum thus obtained was inoculated directly upon nutrient agar agar and into nutrient gelatin. In two or three cases where a slight flow of blood was caused by the puncture, the blood itself was inoculated into tubes of agar agar and of gelatin.

All the agar tubes inoculated with serous fluid furnished luxuriant growths, not differing materially from the growth of anthrax upon agar. None of the inoculations upon agar with blood from the vesicles furnished any indications of development even upon long standing; and none of the inoculations in gelatin, either with serum or with blood, showed the slightest evidence of growth. Furthermore, at the time the pustule was removed by operation, cultures were made from the blood flowing from the wound. These blood cultures also remained perfectly sterile. In view of the results I obtained later, which furnished proof of the presence of the anthrax bacillus in the serous fluid, two things became evident:

(1) That there must have been associated with the anthrax bacillus other organisms, or some substance not an organism, which, while permitting the development of anthrax upon agar, entirely inhibited its growth in gelatin, permitting the deduction that it might also in the same manner inhibit its growth in the tissues of the patient.

(2) That in the particular and minute quantity of blood which was inoculated upon agar and into gelatin no anthrax bacilli were present, since, if present, it would have developed in gelatin or upon agar, thereby furnishing evidence for the belief that no anthrax bacilli were present in the blood of the patient.

From one of the original serum cultures upon agar gelatin-plate cultures were made, with the hope that, under the more favorable conditions of the "plate," development would ensue, and thus make it possible to obtain pure colonies of such organisms as might be present. Although the first, second, third and fourth attenuations were



FIG. 2.—A case of Anthrax.

plated, not the slightest indication of development took place after remaining in the moist chamber for weeks. This confirms the statement made above, that there must have been something present in the culture which entirely prevented the development of the anthrax bacillus upon gelatin.

An abrasion was made at the base of the tail of a mouse, into which a small amount of an agar culture was transferred by means of a platinum wire. The mouse took every means at its command to rid itself of the inconvenience of the treatment, and with apparent success, for no sickness was evident after four days' confinement, at which time the animal was killed by other means.

A second mouse was inoculated with a portion of the same culture diluted with sterilized water, and introduced subcutaneously. The animal died in three days, and on removal the viscera were found soft and pulpy, much engorged, and the spleen enlarged. A microscopic examination of the blood showed myriads of bacilli. From all the organs cultures were made upon agar agar and gelatin. Those made upon agar developed only slightly, owing, doubtless, to the use of agar which had been prepared for a special purpose without the usual addition of meat-juice and peptone.

The gelatin cultures all showed a strong growth along the line of inoculation, and eventually liquefied completely, without, however, previously showing the characteristic anthrax development. Small pieces of the viscera were thrown into tubes of gelatin, previously melted, and the gelatin again solidified by cooling. In three tubes appeared thread-like ramifications distinctly like the anthrax growth, but without the regularity of a line culture. This was especially noticeable in the tube containing the piece of kidney.

A small quantity of the blood of this second mouse was at once inoculated into a guinea-pig. The pig died in almost precisely twenty-four hours, no sickness being apparent until about three hours before death. The microscope revealed myriads of bacilli in the blood. Culture upon agar did not develop, owing, again, to the lack of nutritive material. Culture in gelatin, however, developed quickly and strongly, but without the feather-like appearance of anthrax. The gelatin soon liquefied.

Blood from the first guinea-pig was inoculated into a second guinea-pig, and again death took place in almost precisely twenty-four hours, and under the same conditions. The blood was examined, cultures were made upon agar and gelatin, and with the same

result as furnished by guinea-pig No. 1, except for the important difference furnished by the gelatin culture from the kidney and lung, which presented in the most perfect manner the characteristic feathery growth of anthrax. As the culture from the kidney of each animal was in all cases the most characteristic, an inoculation of the urine, which was smoky, of guinea-pig No. 2 was made into gelatin. It remained sterile.

The published descriptions of the growth of the anthrax bacillus state that the feathery appearance of anthrax in gelatin is best obtained by the use of nutrient gelatin containing 8 per cent. of gelatin. The gelatin used by me was 15 per cent., and out of many cultures made but two were satisfactory, and even on diluting this gelatin with sterilized distilled water, furnishing tubes varying in gelatin contents from 5 to 10 per cent., the desired growths were not again obtained. The difficulty is probably wholly a mechanical or manipulative one, but an obstacle which stands in the way of the ready and certain identification of the anthrax bacillus.

The filaments which shoot out from the inoculation line are fine and tender, and a heavy gelatin naturally retards or wholly prevents their proper development. The anthrax bacillus is also an aerobic organism, so that a permanent inoculation line becomes desirable. Such a line is obtained by the use of a moderately firm gelatin and a needle of large rather than small diameter.

The tubes of low gelatin percentage favorable to the formation of filaments are unfavorable to a permanent inoculation line, a slight rise in temperature being almost sure to nearly or wholly obliterate it.

Immediately after removal of the malignant pustule I took the mass to Dr. Mallory, Assistant Pathologist of the Boston City Hospital, and requested him to ask Dr. Jackson to make a bacteriological examination of the growth to determine, first, whether all the malignant pustule had been removed; and, second, to ascertain, if possible, at what points in the mass the greatest and smallest number of bacilli existed. The pathological report of Dr. Mallory and the bacteriological report of Dr. Jackson will follow.

The following is the report of Dr. Frank B. Mallory, received on March 9, 1892:

The indurated piece of skin received from Dr. Burrell on February 13, 1892, showed a purplish area about one and one-quarter inches in diameter, consisting of a small, central, brownish-black crust sur-

rounded by vesicles of various sizes. On section the tissue was œdematous, and showed numerous small hæmorrhages. Microscopic examination of the tissue (hardened one week after removal) showed marked round-cell infiltration in the region of the crust; in the same place for a short distance only beneath the epidermis, and to a less extent in and beneath the vesicles, were found numerous characteristic anthrax bacilli. None were found in the deeper tissues beneath the epidermis surrounding the pustule, or in the blood present in the blood-vessels.

A guinea-pig inoculated by Dr. Jackson with serum from the vesicles died in two and one-half days. Anthrax bacilli in enormous numbers were found in the blood, lungs, liver and spleen.

Diagnosis, malignant pustule.

The following is the report of Dr. Henry Jackson, Physician to Out-patients of the Boston City Hospital:

On February 13, 1892, at 3 P.M., I received a specimen of skin which had been removed from the side of the neck of a man at the Boston City Hospital by Dr. Burrell. The skin on the edge of the specimen appeared normal; in the centre of the specimen there was a deep, bluish, dry excoriation; surrounding this excoriation were numerous vesicles filled with a clear serum. The tissue underlying the vesicles was of a dull, bluish-red color, as if it were filled with blood.

I made cover-glass preparations from the contents of one of the vesicles, and from the deepest part of a fresh cut made in the under surface of the specimen. These specimens I stained with fuchsin. In the preparation from the vesicle were numerous large rods; the preparation from the deeper tissue showed no rods.

One rabbit and one guinea-pig were inoculated subcutaneously from the fresh cut made in the under surface of the specimen. As I found so few bacilli in the preparations made from the deeper structures of the skin, I inoculated the guinea-pig on February 14 from a vesicle. On February 15 there was some swelling about the point of inoculation in the guinea-pig, otherwise the animal ate well, and did not appear sick until the afternoon of February 16; then the animal was very quiet and did not eat. February 17 the guinea-pig was found dead.

Autopsy.—Four cultures made from the heart blood.

Cover-glass preparations made from the heart blood, liver and spleen contained an enormous number of large bacilli like the bacilli of anthrax. Spleen much swollen, dark red, soft; liver, lungs and kidney engorged with blood. No hæmorrhages found.

Sections made from the lungs, spleen, liver and kidneys showed an enormous number of bacilli, as found in the blood. In many instances the capillaries were so full of bacilli that the walls had ruptured, and small hæmorrhages had taken place into the surrounding tissue. I found the most satisfactory stain to demonstrate the bacilli in the tissues was the "Weigert fibrine stain."

By this method the bacilli are beautifully stained, and the preceding carmine stain shows finely the anatomical distribution of the bacilli.

Culture.—In all the tubes inoculated from the heart blood bacilli of anthrax grew. The characteristic feather-like growth in gelatin was developed in only a few of the gelatin tubes. The cultures were carried on to several generations.

March 10 I made an agar plate-culture from a culture which contained abundant spore formation. After twenty-four hours at 37° C. there were many colonies of anthrax bacilli. No contamination developed.

March 11 I inoculated subcutaneously a guinea-pig from one of the colonies on the agar plate. March 13 the guinea-pig was found dead. The body was still warm. Death occurred in less than forty-eight hours.

Autopsy.—The point of inoculation was swollen; no pus; the gland nearest the point of inoculation was swollen and contained several hæmorrhages; spleen enlarged, soft, dark purple. No hæmorrhages in gastro-intestinal tract. Liver and kidneys engorged with blood. Lungs showed numerous small hæmorrhages; in both posterior lobes of the lungs a spot of consolidated tissue about the size of a pea. These spots were hæmorrhagic. Cover-glass preparations made from the heart blood, spleen and liver showed an enormous number of large bacilli. Cultures were made from the heart blood; bacilli of anthrax developed in all the cultures.

Skin Removed from the Patient.—I made sections from the skin removed by operation. Many of the sections showed no bacilli, or only a few. In some of the sections I found a few small areas in which were numerous bacilli. Where found, the bacilli were situated either in the vesicles on the surface or in new-formed granu-

lation tissue surrounding the hair follicles. No bacilli were found in any of the sections in the deeper portion of the tissue removed. Just beneath the skin were numerous small areas of hæmorrhagic infiltration. The outer portion of the tissue, however, showed no abnormal appearance.

The microscopic examination of the tissue removed demonstrated conclusively the wisdom of an early and free excision of the initial lesion of anthrax in the human subject, as no bacilli and no pathological changes were found except just beneath the vesicles evident before excision. In this case, certainly at the time of the operation, the bacilli had not entered the general circulation.

Résumé.—Large bacilli were found in the vesicles on the skin removed by operation. A guinea-pig inoculated from a vesicle died in three days, and a microscopic examination showed all the appearance of anthrax. Cultures of anthrax bacilli were made from the first guinea-pig.

After one month a second guinea-pig was inoculated with a culture which had been carried on for several generations. The second guinea-pig died in two days with the characteristic lesion of anthrax. Anthrax bacilli were cultivated from the second guinea-pig. (The rabbit inoculated from the original skin on February 13 remained well, and was accidentally killed three weeks after operation.)

From data given in the *résumé* the diagnosis is made of anthrax, malignant pustule, in the specimen of skin.

REMARKS.

During the past five years a new history of this disease is to be recorded. The literature of the subject may be considered under the following headings :

- (1) The localization of the anthrax bacillus.
- (2) Internal anthrax.
- (3) The diagnosis of charbon.
- (4) Immunity by inoculation.
- (5) Prophylaxis.
- (6) The treatment by the injection of other organisms.
- (7) The radical treatment which has come forward with the advent of antiseptics.

The Localization of the Anthrax Bacillus.—The best observers differ as to the presence or absence of the anthrax bacillus in the blood. In some cases where they are found in the various organs far removed from the initial lesion they have not been detected in the blood by the most thorough search. (1) The explanation probably lies in the fact, which appears to have been clearly demonstrated, that the anthrax spores are disseminated through the system by the blood, so that almost any part of the organism may be used as a source of culture even when no bacilli have been found except in the neighborhood of the local lesion. (2) The diffusion of the spores is, however, not inconsistent with the theory of radical local treatment, as the local colony of bacilli are presumably the manufactory of the spores found in other parts of the body.

Internal Anthrax.—The cases in which the lesion is absent altogether, or occurs in a more or less modified form internally, are few, but they are extremely interesting from the difficulty and importance of diagnosis. The most striking cases with which I am acquainted are:

(1) The case of a man in which the attack began suddenly with swelling under the tongue, headache, fever and delirium, and later bloody stools and bloody vomitus appeared, and great dyspnœa. Death occurred on the fourth day (3).

(2) A baby five months old, supposed to have a severe bronchitis. The chest yielded all the physical signs of bronchitis, but in addition there was some general œdema, and an erythematous patch upon the upper left chest. After death, on the ninth day, the "pustules" were found in the bronchi. (4).

(3) A case has been recently reported in which a diagnosis of intestinal obstruction was made by competent surgeons. The patient was so nearly moribund that an operation was not attempted. The autopsy showed great congestion of the intestines; the mesenteric glands were greatly enlarged. (5) In this case the bacilli were abundant in the blood, one loop of intestine was very much swollen, and a thrombus twenty centimetres long was found in the immediate neighborhood.

(4) From the four cases reported by Massing, it appears that vomiting, diarrhœa and extreme constipation may or may not

be present in abdominal anthrax, and that all the symptoms are uncertain. (6)

Even where there is an external lesion the diagnosis may be far from simple. The great variety which the local manifestation may assume is shown in the accompanying analysis of the forms of lesion by Sabatier: (7)

CLASSIFICATION OF SABATIER.

Charbons externes	Formes papuleuses.	Pustule malignant de millet.
	Formes phlyctenoïdes.	<ul style="list-style-type: none"> Pustule malignant classique. Pustule à œdème séparé. Observation personnel.
	Formes œdémateuses.	<ul style="list-style-type: none"> Œdème malin charbonneux bourgeois d'Etampes.
	Pénétration par.	<ul style="list-style-type: none"> Plaie carbonisée. Admise par Roscol, sont à reviser. Point gangreneux sans phlyctene. Absorption par une muqueuse.
Charbons internes	Charbon malin.	<ul style="list-style-type: none"> Avec tumeur symptomatique. Forme œdémateuse. Observation de Mauverzin, 2.
	Fièvre charconneuse,	<ul style="list-style-type: none"> Salmen et Mannaury. Pas de charbons extérieur.
	Mycose intestinale.	
	Forme pulmonaire d'Eppinger.	

And Colin (8) has by experiments on dogs defined clearly ten different forms which the so-called "pustule" may assume.

CLASSIFICATION OF COLIN. FOUNDED ON EXPERIMENTS UPON DOGS.

(1) A small pustule, incompletely formed, which preserves for several days the virulent material.

(2) A diffuse erythema which lasts for a very short time, and vanishes almost suddenly.

(3) A small malignant pustule, more or less elevated, red,

umbilicated, yielding at first a serous, and later a sero-purulent fluid.

(4) A simple œdema without change in the state of the skin.

(5) A pustule followed by œdema.

(6) An œdema followed by a pustule.

(7) A pustule and an œdema arising at the same time.

(8) A pustule with œdema and erythema.

(9) A phlegmonous tumor.

(10) Finally, a small bubo with lymphangitis in the neighborhood.

Immunity by Inoculation.—Woodbridge (9) has obtained immunity from anthrax in animals by the injection of a fluid from which the bacteria after culture have been removed by filtration. The immunity must result from the presence in the fluid of some product of the life of the bacteria.

Hankin (10) has described a distinct chemical substance obtained from the organs of an immune animal—the rat—which possesses the same power.

Prophylaxis.—Inoculation with attenuated cultures of the bacilli themselves has also been used with complete success to confer immunity. But the rarity of the disease in man makes it unlikely that such measures will ever become of practical importance to human patients, except indirectly by decreasing the disease among animals (11).

Treatment by the Injection of Other Organisms.—One of the most curious phenomena in the natural history of the disease is the antagonism of the bacteria of several other diseases to that of anthrax. The researches of a number of eminent bacteriologists have clearly demonstrated the following principles :

(1) That the diplococcus pneumoniæ, the erysipelatous coccus, the staphylococcus pyogenes aureus, the bacillus prodigiosus, and some other forms are hostile to the bacillus of anthrax.

(2) That the growth of anthrax may be retarded or destroyed entirely, according to the quantity of the antagonist injected.

(3) That the injection must be at about the time of infection with anthrax, and that immunity lasts only while the presence of antagonists continues.

(4) The injection of the antagonist may be directly into the circulation, or into the tissues about the pustule. But the first method is no more efficient than the second, and has been followed by death from embolism.

(5) There is danger of death from the antagonist bacillus (12).

Radical Treatment.—The methods of radical treatment which claim attention from the success reported may be enumerated as follows :

(1) The old and obvious method by complete excision.

(2) The use of the actual cautery instead of the knife (13).

(3) The destruction of the lesion by the injection of strong solutions of the most energetic antiseptics, carbolic acid and bichloride of mercury (14).

Ever since Jarnorsky's report of seventy-two cases, all cured by local injection of carbolic acid, this principle of treatment has been extensively followed with results which must be regarded as brilliant, even after every allowance has been made for the irresistible tendency not to report unfavorable cases. More than a hundred cases of cure by this method have been reported, and I have no doubt that the number could be greatly increased by a more complete search.

Antiseptics have been applied in two ways, yielding equally good results. A crucial incision is made and the antiseptic applied in a very concentrated form, or a circle of injections of the germicide is made around the pustule. The effect is the same. The whole mass sloughs off, and the final result in the successful cases is about as radical as an excision. The destruction of the whole pustule by the cautery is only another way of producing the same result. In a number of the cases the local use of powerful antiseptics was supplemented by the internal administration of corrosive or carbolic acid in heroic doses. But the result seems to have been quite as good in the large number of cases in which the treatment was purely local. It cannot be

supposed that enough of the germicide could be taken internally to render all the tissues antiseptic, and on no other supposition can the necessity of the internal treatment be justified. (In some cases the antiseptic, though strong, is said not to have caused a slough.) (15)

Another form of treatment may be noticed in passing. The use of electricity has been repeatedly tried, but, on the whole, without good results. And Apostoli's experiments show that its only means of action is by the acid set free at the positive pole, which he finds destroys the bacillus (16). But the method is less thorough, and more difficult of execution, than the other more radical procedures described. Davies-Colley (17) has reported cures by ipecac in large doses internally and locally applied. His treatment was suggested by Muskett's report of (18) fifty cases without a single death, treated by large doses of ipecac.

Evans (19) has tested this treatment by a bacteriological study in which he has shown that ipecac is fatal to the bacilli in cultures. But the treatment has one serious flaw, if we may judge by Evans's results; the spores are not destroyed. As powerful antiseptics the cautery and the knife would destroy all the local spores. They are in this respect more thorough, and to be preferred.

CONSIDERATION OF CLINICAL HISTORY; PATHOLOGICAL AND BACTERIOLOGICAL REPORTS, AND LITERATURE OF THE SUBJECT.

The points of interest in this case, as they presented themselves to the writer, are the completeness of the history of infection; the recognition of the disease by Dr. Monks; the severity of the man's illness; the increase of the systemic poisoning upon the sixth day of the disease; the relief which was given the patient by the excision of the pustule; the rapid subsidence of the glandular swelling, and his complete recovery. The reports of Mr. Tucker and Drs. Mallory and Jackson are filled with interesting points, especially when their reports and the clinical history are considered in the light of the literature of the subject.